

Place in the file history of the subject Application a marked-up version of Page 1 (attached hereto) showing a new Title and showing status of parent applications.

USE OF PROPARGYL GLYCINE AMINO PROPARGYL DIOL
COMPOUNDS FOR TREATMENT OF [HYPERTENSION] RENAL FAILURE

RELATED APPLICATIONS

5 [This application is a continuation-in-part of Application
Serial No. 07/784,272, filed on 29 October 1991.] This application
is a divisional of U.S. Application Serial No. 09/479,280, filed 6
January 2000, which issued as U.S. Patent No. 6,342,624, which is a
10 continuation of Application Serial No. 09/969,522 filed on 13
November 1997, which is a continuation of Application Serial No.
08/771,334, filed on 16 January 1996, which is a continuation of
Application Serial No. 08/199,237, filed 28 February 1994, which
15 issued 16 January 1996 as U.S. Patent 5,484,812, which is a
continuation-in-part of Application Serial No. 07/784,272, filed on
29 October 1991, which issued on 29 June 1993 as U.S. Patent
No. 5,223,535.

FIELD OF THE INVENTION

20 Renin-inhibiting compounds are known for control of
hypertension. Of particular interest herein are compounds useful as
renin inhibiting agents.

BACKGROUND OF THE INVENTION

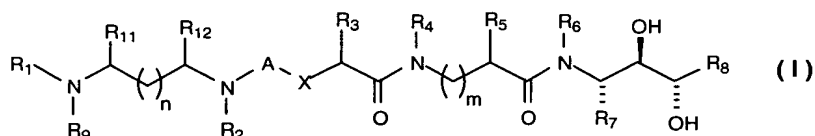
25 Renin is a proteolytic enzyme produced and secreted into
the bloodstream by the juxtaglomerular cells of the kidney. In the
bloodstream, renin cleaves a peptide bond in the serum protein
angiotensinogen to produce a decapeptide known as angiotensin I. A
second enzyme known as angiotensin converting enzyme, cleaves
30 angiotensin I to produce the octapeptide known as angiotensin II.
Angiotensin II is a potent pressor agent responsible for
vasoconstriction and elevation of cardiovascular pressure. Attempts
have been made to control hypertension by blocking the action of
renin or by blocking the formation of angiotensin II in the body
35 with inhibitors of angiotensin I converting enzyme.

Classes of compounds published as inhibitors of the
action of renin on angiotensinogen include renin antibodies,
pepstatin and its analogs, phospholipids, angiotensinogen analogs,
40 pro-renin related analogs and peptide aldehydes.

USE OF PROPARGYL GLYCINE AMINO PROPARGYL DIOL COMPOUNDS
FOR TREATMENT OF [HYPERTENSION] RENAL FAILURE

ABSTRACT

Compounds characterized generally as propargyl glycine amino propargyl diol derivatives are useful for treatment of [hypertension] renal failure. Compounds of particular interest are those of Formula I



wherein A is selected from CO and SO₂ wherein X is selected from oxygen atom and methylene; wherein each of R₁ and R₉ is a group independently selected from hydrido, methyl, ethyl, n-propyl, isopropyl, benzyl, b, b, b-trifluoroethyl, t-butyloxycarbonyl and methoxymethylcarbonyl, and wherein the nitrogen atom to which R₁ and R₉ are attached may be combined with oxygen to form an N-oxide; wherein R₂ is selected from hydrido, methyl, ethyl and isopropyl; wherein R₃ is selected from benzyl, cyclohexylmethyl, phenethyl, imidazolemethyl, pyridylmethyl and 2-pyridylethyl; wherein each of R₅ and R₈ is independently propargyl or a propargyl-containing moiety; wherein R₇ is cyclohexylmethyl; wherein each of R₄ and R₆ is independently selected from hydrido and methyl; wherein each of R₁₁ and R₁₂ is independently selected from hydrido, alkyl and phenyl; wherein m is zero; and wherein n is a number selected from zero through three; or a pharmaceutically-acceptable salt thereof.